

**AMENDMENTS TO THE CLAIMS**

Please replace all prior versions and listings of claims in the application with the following list of claims:

1. (Withdrawn) A method for increasing the concentration of gelsolin or functionally equivalent peptide fragment thereof, in blood or extracellular fluid of a patient *in vitro* or *in vivo*, wherein such increased concentration of gelsolin is needed, said method comprising administering to the patient's blood or extracellular fluid a therapeutically effective amount of gelsolin, or functionally equivalent peptide fragment thereof, under conditions suitable for gelsolin binding.

2-26. (Cancelled)

27. (Withdrawn) The method of claim 1, wherein following administration of the therapeutically effective amount of gelsolin, or functionally equivalent peptide fragment thereof, under conditions suitable for gelsolin binding, the patient's blood or extracellular fluid comprises an increased concentration of gelsolin, as compared with the level of gelsolin before administration, said gelsolin comprising plasma gelsolin, recombinantly produced plasma gelsolin, or expressed plasma gelsolin, or functionally equivalent peptide fragment thereof comprising at least amino acid residues 160-169 of gelsolin, or comprising SEQID No: 1.

28. (Withdrawn) The method of treating a patient in accordance with claim 1, wherein the therapeutically effective amount of gelsolin, or functionally equivalent peptide fragment thereof, is administered *in vivo* to the patient under conditions suitable for gelsolin binding.

29. (Withdrawn) The method of claim 27, wherein the therapeutically effective amount of gelsolin, or functionally equivalent peptide fragment thereof, is administered *in vivo* to the patient, and wherein the increased concentration of gelsolin in the patient protects the patient from

endotoxemia or endotoxin-induced sepsis, or is sufficient to neutralize or reduce endotoxemia or endotoxin-induced septic shock.

30. (Withdrawn) The method of claims 27, wherein endotoxemia or endotoxin-induced sepsis in the patient is LPS-induced following the bacterial infection or triggering of endotoxins in the patient's blood or extracellular fluid.

31. (Withdrawn) The method of claim 30, further comprising decreasing the concentration of bacterial lipopolysaccharide (LPS) released from the infecting gramnegative bacteria into blood or extracellular fluid of the patient and the patient is subject to or susceptible to bacterially produced LPS when the LPS concentration is increased above pre-infection concentrations, said method comprising administering a therapeutically effective amount of gelsolin, or functionally equivalent peptide fragment thereof, that is sufficient to decrease the concentration of bacterial LPS *in vitro* or *in vivo* in the patient's blood or extracellular fluid.

32. (Withdrawn) The method of claim 31, wherein the therapeutically effective amount of gelsolin, or functionally equivalent peptide fragment thereof, is administered *in vivo* to the patient, and wherein the increased concentration of gelsolin in the patient is sufficient to decrease the concentration of bacterial LPS.

33. (Withdrawn) The method of claim 27, further comprising blocking, reducing, ameliorating or preventing bacterial LPS-induced disruption of the patient's cellular responses or formation of toxic structures, wherein the patient's cells are, or will be, exposed to increased levels of bacterial LPS, said method comprising administering a therapeutically effective amount of gelsolin, or functionally equivalent peptide fragment thereof, that is sufficient to affect or block bacterial LPS-induced responses or formation of toxic structures *in vitro* or *in vivo* in the cells.

34. (Withdrawn) The method of claim 33, wherein the increased concentration of gelsolin in the patient reduces, ameliorates, blocks or prevents bacterial LPS-induced disruption of the patent's cellular responses or formation of toxic structures *in vivo* in the patient.

35. (Withdrawn) The method of claim 34, further comprising enhancing endogenous LBP-(LPS binding protein) activity, thereby reducing, blocking or preventing incorporation of LPS into lipoproteins of the patient.

36. (Withdrawn) The method of claim 33, further comprising blocking, reducing, ameliorating or preventing secondary tissue injury in a patient resulting from an accumulation of excess bacterial LPS resulting in increased levels of bacterial LPS, said method comprising administering a therapeutically effective amount of gelsolin, or functionally equivalent peptide fragment thereof, that is sufficient to affect or block bacterial LPS-induced responses or formation of toxic structures *in vitro* or *in vivo* in the cells.

37. (Withdrawn) The method of claim 33, wherein the increased concentration of gelsolin in the patient reduces, ameliorates, blocks or prevents the secondary tissue injury in the patient *in vivo*, and the tissue injury is remote from the site of primary infection or trauma.

38. (Withdrawn) The method of claim 37, further comprising enhancing endogenous LBP-(LPS binding protein) activity, thereby reducing, blocking or preventing incorporation of LPS into blood lipoproteins of the patient.

39. (Withdrawn) A method for blocking, reducing, ameliorating or preventing bacterial LPS-induced pathogenesis selected from the group consisting of microvascular dysfunction, inflammation-induced pulmonary microvascular dysfunction or adult respiratory distress/multiple organ dysfunction syndrome (ARDS), platelet agglutination, thrombus development, venous obstruction, endothelial injury; pulmonary microthrombi, and/or organ injury at sites remote from

primary trauma in a patient resulting from an accumulation of excess bacterial LPS or endotoxins triggered thereby, said method comprising administering under conditions suitable for gelsolin binding a therapeutically effective amount of gelsolin, or functionally equivalent peptide fragment thereof, that is sufficient to block, reduce, ameliorate or prevent said pathogenesis.

40. (Previously presented) A method for restoring or maintaining normal aggregation of platelets in the blood or extracellular fluid of a patient *in vitro* or *in vivo*, wherein the patient is subject to or susceptible to LPS-induced generalized coagulation dysfunction, said method comprising administering to the patient's blood or extracellular fluid a therapeutically effective amount of gelsolin, or functionally equivalent peptide fragment thereof, under conditions suitable for gelsolin binding, thereby affecting platelet function.

41. (Previously presented) The method of claim 40, wherein following administration of the therapeutically effective amount of gelsolin, or functionally equivalent peptide fragment thereof, the patient's blood or extracellular fluid comprises an increased concentration of gelsolin, as compared with the level of gelsolin before administration.

42. (Previously presented) The method of claim 41, wherein the increased concentration of gelsolin in the patient restores or maintains normal aggregation of platelets *in vivo* in the patient, who is otherwise subject to or susceptible to LPS-induced generalized coagulation dysfunction.

43. (Withdrawn) A method of blocking, reducing, ameliorating or preventing fibrinolysis by excess, extracellular free actin in blood or extracellular fluid of a patient *in vitro* or *in vivo*, wherein the patient is subject to or susceptible to excess free actin, comprising administering to the patient's blood or extracellular fluid a therapeutically effective amount of at least one actin-binding compound comprising gelsolin, or functionally equivalent peptide fragment thereof, under conditions suitable for gelsolin binding, thereby binding extracellular free actin.

44. (Withdrawn) A method of predicting an adverse clinical outcome associated with massive gram negative bacterial-caused inflammation in a patient susceptible to inflammatory shock or

endotoxin-induced sepsis, said method comprising measuring the circulating gelsolin concentration in the patient, wherein a decrease  $< 30\%$  of normal, pre-trauma or pre-infection gelsolin levels predicts such adverse outcome and predicts a need for gelsolin therapy.

45. (Withdrawn) The method of claim 44, further comprising using fluorescent phosphorylated inositol phospholipid derivatives or tritium labeling for detecting endotoxins *in vitro* in a blood or fluid sample from the patient.

46. (Withdrawn) A pharmaceutical composition for use in the method of claim 27 comprising:

- (1) gelsolin, or functionally equivalent peptide fragment thereof, wherein such gelsolin or said fragment is substantially free of natural contaminants; and
- (2) a pharmaceutically acceptable vehicle.

47. (Withdrawn) The pharmaceutical composition of claim 46, further comprising adding sufficient amount of  $\text{Ca}^{2+}$  to activate the binding capability of gelsolin, if sufficient  $\text{Ca}^{2+}$  is not available.